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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,304	02/21/2001	Christopher Silvia	018512-00041	3840

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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application N .	Applicant(s)	
	09/623,304	SILVIA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

--The MAILING DATE of this communication appears on the c ver sheet with the c rrespondence address --

THE REPLY FILED 18 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-4,6 and 7*.

   Claim(s) withdrawn from consideration: _____.

Elyabth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1-4 and 6-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Claims 1-4 and 6-7 are also rejected under 35 U.S.C. 112 first paragraph. The basis for these rejections are set forth at pg 3-7 of the previous Office Action (Paper No. 20, 16 June 2003). Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Applicant asserts that an absolute negative control, i.e., cells expressing neither Kir5.1 nor Kir4.1, is not necessary for the experiment illustrated in Figure 1 and Example II to demonstrat the functions of the Kir5.1 polypeptide. Applicant states that because the Kir5.1 functionality is shown through comparison of current magnitude between the same host cells in which exogenous Kir5.1 alone or Kir5.1 plus Kir4.1 are introduced and expressed, the endogenous expression of Kir5.1 or Kir4.1 and any potential effects from such expression are background and thus bears no relevance to the final results of the experiment. Applicant submits that the experiment demonstrating Kir5.1 activity is scientifically valid and that the asserted utility based on Kir5.1 activity is specific. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, it is not clear from Example II (pg 57) or Figure 1 if the Kir5.1 alone is homomeric, and if so, what the significant difference is between Kir5.1 alone and mixtures or dimers of Kir5.1 and Kir4.1. Also, it cannot be determined from Example II or Figure 1 what role Kir4.1 has in current magnitude changes in combination with Kir5.1. For example, is Kir4.1 only (although added to Kir5.1) causing the increase in current magnitude? A control sample with Kir4.1 alone would have been appropriate to indicate that the addition of Kir5.1 to Kir4.1 does indeed cause an increase in current magnitude above that of Kir4.1 alone.

Applicant believes that the Examiner was questioning the credibility of the asserted utility of using Kir5.1 channel as a target for treating diseases, and not whether the asserted utility is specific or substantial. It is noted that the Examiner has not questioned the credibility of the above-mentioned asserted utility, but rather, has indicated that the utility is not specific or substantial. See the last paragraph on page 5 of the previous Office Action (Paper No 20, 16 June 2003).

Applicant argues that Example 8 the Revised Interim Utility Guidelines Training Materials can be compared to the instant application. Applicant indicates that the present application claims nucleic acids encoding Kir5.1 potassium channels, which are analagous to compound A that inhibits enzyme XYZ. Applicant's arguments have been fully considered but are not found to be persuasive. The fact pattern in the instant application is not analogous to Example 8 in the Revised Interim Utility Guidelines. In Example 8 of the Guidelines, enzyme XYZ i a well-known tyrosine kinase, the substrate for the enzyme and the reaction which the enzyme catalyzes are wel known. Therefore, an inhibitor of enzyme XYZ, compound A, would have a well-established utility in controlling the enzyme/substrate interaction. However, the structure and function of the nucleic acid molecule of the instant application is not known, and therefore has no credible, specific and substantial asserted utility or a well established utility.

Applicant contends that the skilled practitioner would appreciate that the Kir 5.1 channel to be an inward rectifyin potassium channel useful for modulating cell excitability and membrane potential. Applicant submits that the claimed nucleic acids encode an inwardly rectifying potassium channel useful for modulating cell excitability. Applicant also indicates that because the Kir5.1 channel is capable of modulating cell excitability, the Kir5.1 channel is a useful target for the treatment of diseases and conditions related to cell excitability. No substantially new arguments regarding this issue have been presented, and thus the rejections are maintained for reasons of record.

Furthermore, claims 1-4 and 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Stringency is relative, and the art does not recognize a single set of conditions as stringent. The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions (e.g., "hybridizes at wash conditions of A X SSC and B % SDS at CoC"), claims 1-4 and 6-7 fail to define the metes and bounds of the varying structures of polynucleotides recited. The basis for this rejection is set forth at pg 7-8 of the previous Office Action (Paper No. 20, 16 June 2003). Applicant argues that there are

many optional ingredients that can be included in the hybridization and wash solutions without altering the stringency of a hybridization. Applicant submits that even if any additional monovalent cations may be included i the hybridization solution as recited in claim 1, the level of stringency will not be significantly effected. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the terms "comprise/comprising" still encompasses various unknown stringency conditions, which would allow for the stringency to be lowered before hybridization has ended. This would produce polynucleotide variants other than Kir5.1.